NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Tocilizumab for the treatment of juvenile idiopathic arthritis

Draft Scope

Remit / appraisal objective

To appraise the clinical and cost-effectiveness of tocilizumab within its licensed indication for juvenile idiopathic arthritis.

Background

Juvenile idiopathic arthritis (JIA) is a term that covers a heterogeneous group of syndromes in which the onset of inflammatory arthritis occurs before the age of 16 years and lasts for more than 6 weeks. JIA is characterised by persistent joint swelling, pain and limitation of movement. The cause of JIA is poorly understood, but may relate to genetic and environmental factors.

A classification system for JIA has been developed by the International League of Associations for Rheumatology (ILAR). There are seven categories of JIA: systemic, oligo arthritis (formerly pauciarticular), polyarthritis rheumatoid factor positive, polyarthritis rheumatoid factor negative, enthesitis related arthritis, psoriatic arthritis and unclassified (types that do not correspond to any, or to more than one, category). The clinical manifestations and severity of the different sub-types varies considerably. Systemic onset JIA is a multiorgan disease characterised by arthritic symptoms, fever, transient rash, liver and spleen enlargement. Approximately a third of children with systemic onset JIA develop severe resistant polyarticular arthritis.

JIA can lead to growth retardation, joint contractures, eye problems, destructive joint disease requiring joint replacements, and permanent disability. JIA can impair children's personal and social functioning and development. Children often miss out on schooling and normal childhood activities, and as adults they may be limited in, or unable to work. It may also have a considerable impact upon the family of the child.

JIA is a relatively rare disease, with an estimated incidence in the UK of 0.1 per 1000 children, equivalent to 1000 children diagnosed per year. The prevalence is in the order of 1 per 1000 children, and about 10,000 children in the UK are affected. Approximately 10% of children diagnosed with JIA have systemic onset disease.

Treatment aims to control pain and inflammation, and reduce joint damage, disability and loss of function, thereby improving quality of life. The standard treatment for systemic onset JIA includes combinations of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, corticosteroids and disease modifying anti-rheumatic drugs (DMARDs). Methotrexate is often used as initial therapy when DMARDs are considered necessary, although no DMARD

is licensed for use in children in the UK. There are currently no biologics licensed in the UK for the treatment of systemic onset JIA in children and young people. Non-drug therapies include surgery and physical therapy.

NICE has issued guidance (technology appraisal 35) on the use of etanercept for the treatment of polyarticular JIA.

The technology

Tocilizumab (RoActemra, Roche Products) is a humanised monoclonal antibody that inhibits the activity of the cytokine interleukin-6 (IL-6). IL-6 is a pro-inflammatory mediator. It has been hypothesised that the over-expression of IL-6 in systemic onset JIA is one of the factors responsible for the damaging processes which affect articular cartilage and bone. Tocilizumab is administered intravenously.

There is currently no UK marketing authorisation for the use of tocilizumab for the treatment of systemic onset JIA. It has been studied in children and young people older than 2 years with systemic onset JIA which has responded inadequately to previous therapy with one or more NSAIDs and systemic corticosteroids. It has been studied as a monotherapy or in combination with methotrexate compared with placebo.

Interventions	Tocilizumab monotherapy Tocilizumab in combination with methotrexate
Population	Children and young people older than 2 years with systemic onset JIA
Comparators	• Conventional DMARDs
Outcomes	Outcomes to be considered include: • disease activity • physical function • joint damage • pain • steroid sparing • mortality • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The time horizon for the economic evaluation should reflect the chronic nature of the condition. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations:	Related Technology Appraisals: Technology Appraisal No.35, March 2002, 'The use of etanercept for the treatment of juvenile idiopathic arthritis'. Static guidance. Ongoing Technology Appraisals: Technology Appraisal in Preparation (suspended) 'Adalimumab for the treatment of juvenile idiopathic arthritis'.

Questions for consultation

Has the population in the scope been defined appropriately? Should the population be further specified by previous therapy with NSAIDs and systemic corticosteroids?

Have the most appropriate comparators for the treatment of systemic onset JIA been included in the scope? Are the comparators listed routinely used in clinical practice?

- Which DMARDs are used in current clinical practice for this population?
- Should best supportive care be included? If yes, how should best supportive care be defined?
- Should stem cell transplant/surgery be included as a comparator?
- Should biological agents, such as etanercept, adalimumab, anakinra and abatacept be included as comparators?
- Should tocilizumab monotherapy be compared with tocilizumab in combination with methotrexate?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.